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FILE 'CAPLUS' ENTERED AT 15:04:41 ON 16 JUL 2003
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FILE 'BIOSIS' ENTERED AT 15:04:41 ON 16 JUL 2003
COPYRIGHT (C) 2003 BIOLOGICAL ABSTRACTS INC.(R)

=> ribavirin
L1        5560 RIBAVIRIN

=> "viral antigen"
L2        8984 "VIRAL ANTIGEN"

=> L1 and L2
L3          25 L1 AND L2

=> HCV (l) L3
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HCV (L) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HCV (L) L8'
L4           5 HCV (L) L3

=> HBV (l) L3
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HBV (L) L7'
PROXIMITY OPERATOR LEVEL NOT CONSISTENT WITH
FIELD CODE - 'AND' OPERATOR ASSUMED 'HBV (L) L8'
L5           0 HBV (L) L3

=> D L4 IBIB TI SO AU ABS 1-5
```

```
> HCV adj vaccine
          6665 HCV
            17 HCVS
          6669 HCV
                 (HCV OR HCVS)
           209 ADJ
         38893 VACCINE
         39204 VACCINES
         48795 VACCINE
                 (VACCINE OR VACCINES)
L6           0 HCV ADJ VACCINE
                 (HCV(W)ADJ(W)VACCINE)

=> " HCV immunogenci compostion"
          6665 "HCV"
            17 "HCVS"
          6669 "HCV"
                 ("HCV" OR "HCVS")
             0 "IMMUNOGENCI"
            21 "COMPOSTION"
             4 "COMPOSTIONS"
            24 "COMPOSTION"
                 ("COMPOSTION" OR "COMPOSTIONS")
L7           0 " HCV IMMUNOGENCI COMPOSTION"
                 ("HCV"(W)"IMMUNOGENCI"(W)"COMPOSTION")

=> "DNA vaccine"
        618054 "DNA"
         16409 "DNAS"
        620571 "DNA"
                 ("DNA" OR "DNAS")
         38893 "VACCINE"
         39204 "VACCINES"
         48795 "VACCINE"
                 ("VACCINE" OR "VACCINES")
L8        2411 "DNA VACCINE"
                 ("DNA"(W)"VACCINE")

=> HCV and L8
          6665 HCV
            17 HCVS
          6669 HCV
                 (HCV OR HCVS)
L9          57 HCV AND L8

=> plasmid and L9
         98273 PLASMID
         39255 PLASMIDS
        109918 PLASMID
                 (PLASMID OR PLASMIDS)
L10         45 PLASMID AND L9

=> NS3 and L10
          1566 NS3
L11          4 NS3 AND L10

=> NS4 and L10
           455 NS4
L12          2 NS4 AND L10

=> ribavirin and L9
          1762 RIBAVIRIN
             1 RIBAVIRINS
          1762 RIBAVIRIN
```

```
                (RIBAVIRIN OR RIBAVIRINS)
L13          0 RIBAVIRIN AND L9

=> ribavirin and L8
          1762 RIBAVIRIN
             1 RIBAVIRINS
          1762 RIBAVIRIN
                (RIBAVIRIN OR RIBAVIRINS)
L14          0 RIBAVIRIN AND L8

=> vector and L9
        123750 VECTOR
         71049 VECTORS
        166171 VECTOR
                (VECTOR OR VECTORS)
L15         32 VECTOR AND L9

=> L15 and NS3
          1566 NS3
L16          2 L15 AND NS3

=> L15 and NS4
           455 NS4
L17          0 L15 AND NS4
```

L16 ANSWER 2 OF 2 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:55855 CAPLUS
DOCUMENT NUMBER: 130:262790
TITLE: Development of a multigenic plasmid **vector** for **HCV** DNA immunization
AUTHOR(S): Papa, S.; Rinaldi, M.; Mangia, A.; Parrella, P.; Signori, E.; Lombardi, L.; Fazio, V. M.
CORPORATE SOURCE: Laboratory for Molecular Oncology and Gene Therapy, IRCCS H., San Giovanni Rotondo, Italy
SOURCE: Research in Virology (1998), 149(5), 315-319
CODEN: RESVEY; ISSN: 0923-2516
PUBLISHER: Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Hepatitis C virus (**HCV**) viral nucleocapsid protein (C), non-structural protein 3 (**NS3**) and the envelope glycoproteins E1 and E2 are candidate immune targets for developing anti-**HCV** **DNA vaccine**. Nevertheless, the immune response elicited by these antigens often appears weak and/or transient. Different approaches have been studied for enhancing and/or modulating the immune response of the **DNA vaccine**. On the basis of a prototype multigenic plasmid **vector** constituted of two different transcription cassettes (pRC100), we have developed a plasmid **vector** that allows the independent and simultaneous expression of murine IL2 and of an antigenic domain of the **HCV** **NS3** C terminus (pRC112-**HCV**). The highly conserved **NS3** region spans from nt 4403 to nt 4829 and contains two putative B and T epitopes. The development of this multigenic plasmid **vector** may combine the expression and local prodn. of an immunomodulatory mol. (mIL2) together with the possibility of addressing the host immune response to the most immunogenic and conserved epitopes, specifically tailored in the plasmid **vector**.

REFERENCE COUNT: 24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 2 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2003:281779 CAPLUS
DOCUMENT NUMBER: 138:400058
TITLE: Low dose and gene gun immunization with a hepatitis C virus nonstructural (NS) 3 DNA-based vaccine containing NS4A inhibit NS3/4A-expressing tumors in vivo
AUTHOR(S): Frelin, L.; Alheim, M.; Chen, A.; Soederholm, J.; Rozell, B.; Barnfield, C.; Liljestroem, P.; Saellberg, M.
CORPORATE SOURCE: Division of Clinical Virology, Huddinge University Hospital, Stockholm, S-141 86, Swed.
SOURCE: Gene Therapy (2003), 10(8), 686-699
CODEN: GETHEC; ISSN: 0969-7128
PUBLISHER: Nature Publishing Group
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The hepatitis C virus (**HCV**) protease and helicase encompasses the nonstructural (NS) 3 protein and the cofactor NS4A, which targets the NS3/4A-complex to intracellular membranes. The authors here evaluate the importance of NS4A in NS3-based genetic immunogens. A full-length genotype 1 NS3/4A gene was cloned into a eucaryotic expression **vector** in the form of NS3/4A and NS3 alone. Transient transfections revealed that the inclusion of NS4A increased the expression levels of NS3. Subsequently, immunization with the NS3/4A gene primed 10- to 100-fold higher levels of NS3-specific antibodies as compared to immunization with the NS3 gene. Humoral responses primed by the NS3/4A gene had a higher IgG2a/IgG1 ratio (>20) as compared to the NS3 gene (3.0), suggesting a T helper 1-skewed response. Low dose i.m. (10 .mu.g) immunization with the NS3/4A gene inhibited the growth of NS3/4A-expressing tumor cells in vivo, whereas the NS3 gene alone or NS3 protein did not. The authors then evaluated the efficiency of the NS3/4A gene administered by the gene gun, at the same doses used for humans, in priming cytotoxic T lymphocyte (CTL) responses. Three to 4 4 .mu.g doses of the NS3/4A gene primed CTL at a precursor frequency of 2-4%, which inhibited the growth of NS3/4A-expressing tumor cells in vivo. Thus, NS4A enhances the expression levels and immunogenicity of NS3, and an NS3/4A gene delivered transdermally could be a therapeutic vaccine candidate.

REFERENCE COUNT: 53 THERE ARE 53 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 4 OF 32 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 2002:667612 CAPLUS
DOCUMENT NUMBER: 138:54091
TITLE: DNA-based vaccination against hepatitis C virus (**HCV**): effect of expressing different forms of **HCV** E2 protein and use of CpG-optimized **vectors** in mice
AUTHOR(S): Ma, Xiaoying; Forns, Xavier; Gutierrez, Robin; Mushahwar, Isa K.; Wu, Tong; Payette, Paul J.; Bukh, Jens; Purcell, Robert H.; Davis, Heather L.
CORPORATE SOURCE: Loeb Health Research Institute, Ottawa, ON, K1Y 4E9, Can.
SOURCE: Vaccine (2002), 20(27-28), 3263-3271
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
AB DNA-based immunization may be of prophylactic and therapeutic value for hepatitis C virus (**HCV**) infection. In efforts to improve the immunogenicity of a plasmid expressing the second envelope protein (E2) of **HCV**, we evaluated in mice the role of the antigen localization and demonstrated that membrane-bound and secreted forms induced higher titers of E2-specific antibodies, as well as earlier and higher seroconversion rates, than the intracellular form, but all three forms induced strong CTL. We also investigated whether E2-specific antibody responses could be enhanced by CpG optimization of the plasmid backbone and showed that removal of neutralizing CpG dinucleotides did not have a significant effect but addn. of 64 immunostimulatory CpG motifs significantly enhanced anti-E2 titers. These results may have implications for the design and development of **HCV DNA vaccines**.
REFERENCE COUNT: 82 THERE ARE 82 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 46 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:675335 CAPLUS
DOCUMENT NUMBER: 132:150304
TITLE: **DNA vaccines**
AUTHOR(S): Encke, Jens; Putlitz, Jasper zu; Wands, Jack R.
CORPORATE SOURCE: Molecular Hepatology Laboratory, Massachusetts General Hospital Cancer Center, Harvard Medical School, Boston, MA, USA
SOURCE: Intervirology (1999), 42(2-3), 117-124
CODEN: IVRYAK; ISSN: 0300-5526
PUBLISHER: S. Karger AG
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
REFERENCE COUNT: 78 THERE ARE 78 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 47 OF 57 CAPLUS COPYRIGHT 2003 ACS
ACCESSION NUMBER: 1999:573320 CAPLUS
DOCUMENT NUMBER: 132:77300
TITLE: Characterization of the humoral and cellular immune responses against hepatitis C virus core induced by DNA-based immunization
AUTHOR(S): Hu, Guo-Jun; Wang, Richard Y-H.; Han, Dai-Shu; Alter, Harvey J.; Shih, J. Wai-Kuo
CORPORATE SOURCE: Department of Transfusion Medicine, Warren G. Magnuson Clinical Center, National Institutes of Health, Bethesda, MD, 20892-1184, USA
SOURCE: Vaccine (1999), 17(23-24), 3160-3170
CODEN: VACCDE; ISSN: 0264-410X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
REFERENCE COUNT: 39 THERE ARE 39 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L9 ANSWER 51 OF 57 CAPLUS COPYRIGHT 2003 ACS

ACCESSION NUMBER:	1999:55855 CAPLUS
DOCUMENT NUMBER:	130:262790
TITLE:	Development of a multigenic plasmid vector for **HCV** DNA immunization
AUTHOR(S):	Papa, S.; Rinaldi, M.; Mangia, A.; Parrella, P.; Signori, E.; Lombardi, L.; Fazio, V. M.
CORPORATE SOURCE:	Laboratory for Molecular Oncology and Gene Therapy, IRCCS H., San Giovanni Rotondo, Italy
SOURCE:	Research in Virology (1998), 149(5), 315-319 CODEN: RESVEY; ISSN: 0923-2516
PUBLISHER:	Editions Scientifiques et Medicales Elsevier
DOCUMENT TYPE:	Journal
LANGUAGE:	English
REFERENCE COUNT:	24 THERE ARE 24 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT